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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,730	04/02/2004	James L. Hartley	0942.285000N/BJD/JKM	1581

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EXAMINER	
VOGEL, NANCY S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,730	HARTLEY ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/06, 3/2/05 (2)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending in the case.

Receipt of Information Disclosure Statements on 6/23/06 and 3/2/05 (2).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9-16, are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (WO93/19172) (AO3, cited by applicants).

Johnson et al. disclose a method of cloning an amplification product comprising obtaining an amplification product comprising a first recombination site and a second recombination site which do not recombine with each other; and combining said product with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other, under conditions such that recombination occurs between said first and third and second and fourth recombination sites, thereby producing a product vector (see pages 21-23). At page 22, line 31 – page 23, line 12, it is disclosed that different site specific recombination sites may be used in the first vector, as well as in the second vector, such that there will not be recombination between said sites within each vector, but that each vector has a recombination site that

recombines with a site on the other vector. The reference discloses that the method may be carried out in vitro (see page 21, lines 9-11; see claims). The reference discloses that the first site may be the loxP site, and the second may be the loxP 511 site (page 23, lines 13-22) or attB, attP, attL, attR. The recombinase protein may be Cre, Int, IHF (see pages 29-33). The reference discloses that the vector is an expression vector comprising promoter, origin of replication, selectable marker, and genes (see page 20-23).

Claims 1-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Griffiths et al. (US Patent No. 5,962,255).

Griffiths et al teach a method for cloning an amplified linear nucleic acid by amplifying a nucleic acid template with a first primer comprising a first recombination site and second primer comprising a second recombination site, where the first and second recombination sites do not recombine with each other. The vector comprises third and fourth recombination sites which will recombine with the first and second recombination sites, as recited in the instant claim 1 (see Griffiths at Example 6-7, see claims). Recombining the amplified nucleic acid and a vector in the presence of a recombination protein produces a recombined vector (product vector). Regarding claim 2, the amplification is accomplished by an amplification reaction, which may be via replication in a host cell. Regarding claim 3, the recombined (product) vector is expressed in a host cell. Regarding claims 3-7, the vector comprises a promoter, a restriction site, an origin of replication, a cloning site and a gene. Regarding claim 8, the product nucleic acid is linear. Regarding claims 9-10, the first, second, third or

fourth recombination sites are lox sites or mutants thereof (loxP and loxP511). Regarding claims 11-13, the recombination sites may be lox or att sites (see Griffiths et al, column 19 and Example 6 and claims). Regarding claim 14, the product nucleic acid molecule and said vector are combined in the presence of at least one recombination protein. Regarding claims 15 and 16, the recombinase may be Cre or other recombinases (see col. 19 and 23).

Claims 1-8, 14, 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Griffiths et al (US Patent No.6,010,884; IDS Ref. No. AK3) as evidenced by vector maps obtained from the New England Biolabs and Fermentas websites. Note: Examiner has interpreted "recombination site" to include restriction enzyme sites since the term ~recombination site" has not been defined in the specification.

Griffiths et al teach a method of cloning comprising (a) amplifying a nucleic acid template (NQII) with a first primer comprising at least a first recombination site and a second primer comprising at least a second recombination site, wherein said first and second recombination sites do not recombine with each other; and (b) combining in vitro an amplified DNA product nucleic acid molecule flanked by a first recombination site and a second recombination site, wherein the recombination sites do not recombine with each other, with at least one first vector comprising a third and fourth recombination sites that do not recombine with each other, under conditions such that recombination occurs between said first and third and said second and fourth recombination sites, thereby producing a product vector (see entire document, especially column 16, lines 33-60). Regarding claim 17 and 18, Griffiths et al teach

such a method wherein the amplification is accomplished by an amplification reaction (see, e.g., column 16, lines 50-53). Regarding claim 2, Griffiths et al teach such a method further comprising inserting said product vector into a host cell (see, e.g., column 16, lines 53-60). Regarding claim 3, Griffiths et al teach such a method wherein said first vector is an expression vector (see, e.g., column 16, lines 35-39). Regarding claims 4-7, Griffiths et al teach such a method wherein the vector comprises a promoter (P1ac), an origin or replication (ColEI) and a selectable marker (ampicillin resistance). Regarding claim 14, Griffiths et al teach such a method wherein said product nucleic acid molecule and said vector are combined in the presence of at least one recombination protein inherent in the ligation mixture (see, e.g., column 16, lines 53-57).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 11, 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claims 9, 11, and 13 are drawn to the method of claim 1, wherein said first second, third or fourth recombination sites are lox, att, or FRT sites or functional mutants thereof. While the specification at pages 41-44 describes possible mutations that may be made in recombination sites, there is no description of the structure of mutants other than the loxP511 mutant. The claims contain no limitation as to the structure of the recombination sites that are intended to be encompassed. Claims 9, 11 and 13 are genus claims in terms of a method using DNA comprising recombination sites that are variants or mutants of the known and identified lox, att, or FRT sites, and therefore encompass a broad class of methods using nucleic acid molecules that may have virtually any structure, which retain the function of recombination sites. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods utilizing the encompassed recombination sites based on the teachings of the specification. While the specification provides general information on the sequences of the known loxP, att, and FRT sites, there is no disclosure of the precise nucleotides which must be retained in order for function to be maintained. Further, there is no limitation as to the number of nucleotides which may be altered, and therefore, virtually any nucleotide sequence which results in a functional recombination site, is encompassed, for which description has not been disclosed. Therefore, the

specification does not describe the claimed method utilizing recombination sites which are functional mutants of lox, att, or FRT, in such in such full, clear, concise and exact terms so as to indicate that Applicant has possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite in the recitation of "in vitro" since it is not clear whether it is intended to encompass reactions performed in living cells in a reaction vessel, or a reaction carried out using components isolated from cells in a vessel, or both. Therefore, the intended metes and bounds of the claimed subject matter cannot be determined.

Claims 3-7 are vague and indefinite since it is not clear which vector in claim 1, i.e. that recited in line 5 or line 10, is intended.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 6-18, are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29-34, of U.S. Patent No. 5,888,732. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting patent recites the method of the instant application, except that in part (a) a vector comprising a first recombination site and a second recombination site which do not recombine with each other is recited, rather than an "amplification product" as recited in the instant claims. However, a vector is considered to be encompassed by the term "amplification product" since it is amplified in the cell in which it is produced by the DNA replication process. It is noted that the limitation in the instant claims, whereby the amplification product "is a polymerase chain reaction product" does not change the inherent nature of the product used in the claimed method, which may be a linear DNA molecule. While the conflicting claims do not specify the type of recombination protein or recombination sites, such proteins as Cre, Int, Xis and IHF, and their recombination sites loxP, att, and FRT are well known in the art and further, are set forth in the specification of the conflicting patent as examples

of recombination proteins and recombination sites which are intended to be used in the claimed method (cols. 13-16).

Claims 1-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-20 and 45-55 of U.S. Patent No. 6720140. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent recite the same method as that of the instant claims, except that a mutant recombination site is specified (claims 15-20), or the method further comprises selecting for a host comprising the product molecule using a selectable marker. However the instant claims recite that any recombination site may be used, and claims are also drawn to transforming a host cell with the product vector, in addition to utilizing a selectable marker. Therefore, the claims of the conflicting patent are encompassed by the claims of the instant application.

Claims 1-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 52-59 and 61-67 of copending Application No. 10/680,316. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are either anticipated, or would have been obvious over the reference claims.

The conflicting claims are drawn to the same method as claimed in the instant application, but differ in that the method of obtaining the amplification product is recited. However, the instant application discloses that the amplification product may be obtained by the means of amplification recited in the conflicting application. Therefore,

the starting material, i.e. the amplification product, would be the same as that recited in the instant application. Claims 2-14, 17 and 18 are dependent on the above claim 1 and correspond with dependent claims 53-59 and 61-67.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NV
9/27/06

NANCY VOGEL
PRIMARY EXAMINER